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¹School of Engineering, Griffith University, Southport, Australia, ²The Innovative Cardiovascular Engineering and Technology Laboratory, Critical Care Research Group, The Prince Charles Hospital, Chermside, Australia, ³School of Medicine, University of Queensland, Brisbane, Australia
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Mr Sam Liao¹², Dr Christina Theodoropoulos², Dr Keith Blackwood², Assoc. Prof. Mia Woodruff², Dr Shaun Gregory¹³
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Hyperoxaemia partially preserves collagen-dependent platelet function during extracorporeal membrane oxygenation

Dr Rylan Hayes¹², Mr Charles McDonald¹², Associate Professor Kiran Shekar¹², Professor John Fraser¹²
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Implementation and evaluation of an emergency department nurse navigator role: a controlled observation study utilising mixed methodology

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**Introduction.** Increased recognition of morbidity/mortality related to prolonged Emergency Department (ED) stays has led to novel methods to improve patient flow/compliance with government-set time-targets.

**Methods.** An ED Nurse Navigator (NN) role was implemented during peak activity (12:30-20:30) with a week-off-week-on pattern. Durations between various ED time-points were calculated for all patients that presented during the 20-week study-period and data comparisons conducted for off-weeks versus on-weeks. Qualitative data were collected via multi-disciplinary focus-groups plus NNs maintained a daily diary.

**Results.** Fewer patients experienced a ramp wait-time on NN-on-weeks (47.8%), with ramp times shorter by over 7 minutes (mean difference 7.45, SE 1.36, 95% CI:4.79-10.12; \( t (2005)=5.485, p < 0.001 \)). Time intervals from arrival until various other cut-offs were significantly shorter (see Table). More patients met both 2hr Time To Refer Target (TTRT) and 4hr National Emergency Access Target (NEAT) during on-weeks; latter was statistically significant. Qualitative analysis of diary data revealed the iterative processes of both the Navigator growing into the role and ED staff incorporating the role into flow processes. Focus group participants revealed some initial differences in acceptance of the role between staff groups potentially related to role-boundary confusion but confirmed overall endorsement plus insightful themes relating to optimal implementation.

**Conclusion.** Introduction of a NN may enhance ED flow times and compliance with NEAT targets.

**Paper to practice.** Data supporting health efficiencies is critical for business case requests for funding

<table>
<thead>
<tr>
<th>Time intervals</th>
<th>Navigator WEEK OFF (n)</th>
<th>Navigator WEEK ON (n)</th>
<th>Significance ( p )</th>
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<tr>
<td>Ambulance ramp time</td>
<td>36.97 mins (997)</td>
<td>29.33 mins (903)</td>
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<td>Arrival to treatment</td>
<td>64.65 mins (9754)</td>
<td>62.36 mins (9883)</td>
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<tr>
<td>Arrival to referral request</td>
<td>180.72 mins (6215)</td>
<td>168.02 mins (6507)</td>
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<tr>
<td>Arrival to ready to depart</td>
<td>216.97 mins (9826)</td>
<td>212.11 mins (9951)</td>
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<tr>
<td>ED total length of stay</td>
<td>247.25 mins (9826)</td>
<td>242.54 mins (9949)</td>
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<tr>
<td>NEAT Met</td>
<td>60.1% (5905)</td>
<td>62.2% (6187)</td>
<td>0.003</td>
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<tr>
<td>TTRT Met</td>
<td>45.6% (2832)</td>
<td>47.2% (3073)</td>
<td>0.063</td>
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</tbody>
</table>
Hypoglycaemia: Prevalence and Characteristics in Non-Diabetic Adults with Cystic Fibrosis, attending a centre in Australia

Ms Jenna Stonestreet¹, Dr Monica Wagenaar¹, Mrs Karen Herd¹, Miss Angela Matson¹, Dr Daniel Smith¹, Dr Scott Bell¹
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Introduction. Cystic Fibrosis (CF) patients with exocrine pancreatic insufficiency (PI) have less alpha, beta and pancreatic polypeptide cell function than sufficient patients. No significant association between hypo and development of CF-related diabetes has been found to date. The aim of this project was to review the prevalence and characteristics of hypoglycaemia in non-diabetic adults with CF.

Method. A retrospective audit was performed (2013) including pre transplant CF adults ≥18 years (n=275), excluding diabetic / impaired glucose tolerant patients (n=84). Audit group n=191. Hypoglycaemic patients (plasma glucose ≤ 3.9mmol/l), were compared with normal glucose tolerant (NGT) controls. Additional characteristics of the hypoglycaemia group were summarised.

Results. The prevalence of non-diabetic hypoglycaemia in this group was 10.2%. No differences were identified between hypo and NGT control groups for age, gender, genotype, liver disease and lung function. Mean BMI was significantly less in hypo group (21.96 kg/m² sd3.01) compared to controls (24.04 kg/m² sd 4.63) (p=0.023). The hypo group had significantly higher pancreatic insufficiency (p<0.001). Characteristics of the hypo group: mean onset 21.75years (sd7.09), mean length of diagnosis 5.46years (sd4.56), 89% symptomatic adrenergic reactions, 11% asymptomatic. The most common hypo triggers was fasting/insufficient carbohydrates or delayed meal (61%). 75% of patients received education on the inclusion of regular low glycaemic index carbohydrates and higher protein items to prevent the occurrence.

Conclusion. The prevalence of non-diabetic hypoglycaemia in this group was 10.2%. The hypo group had significantly lower mean BMI and a higher rate of pancreatic insufficiency. This may be due to lack of gluconeogenic reserves and/or pancreatic dysfunction in hypoglycaemic pathophysiology.

Paper to Practice. CF dietitians should determine the reason for hypoglycaemia in non-diabetic CF patients and provide education in order to minimise the risk of them re-occurring.
High-flow oxygen via tracheostomy improves oxygenation in patients weaning from mechanical ventilation.

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Introduction. Weaning tracheostomised patients from prolonged ventilation can be challenging and costly. Transitioning from positive- to negative-pressure ventilation can result in derecruitment and reintubation, leading to higher morbidity and mortality. Current treatment options are low-flow oxygen delivered up to 15 L/min via humidified t-piece (LFT). Humidified high-flow tracheostomy (HFT) delivers a prescribed fraction of inspired oxygen (FiO₂) up to 50 L/min. Data indicate high-flow oxygen via nasal cannulae increases airway pressure and end-expiratory lung volumes (EELV). However, no data exist indicating HFT does similar. Study aims were to assess HFT’s effects on airway pressure, EELV, oxygenation, tidal volume (Vt), respiratory rate and dyspnoea.

Methods. Tracheostomised patients ≥18y ventilated for >96 hours were eligible for inclusion. Using a randomised crossover design, humidified LFO at 15 L/min via t-piece (LFT) was compared to HFT at 50 L/min with FiO₂ titrated to maintain SpO₂≥90%. A 15-minute washout separated 15-minute treatment periods. Univariate and multivariate models were used to test for differences in outcome variables.

Results. Twenty patients, 14 male, were studied. Mean (SD) ventilation time was 16.7 days (7.2) and patients were tracheostomised for a mean 10.8 days (5.7). HFT led to significantly higher SaO₂/FiO₂ ratio when compared with LFT (Mean difference +34.1; 95%CI 17.5, 50.7; P=0.01). HFT generated higher airway pressures than LFT (Mean difference +0.6; 95%CI 0.4, 0.9; P=0.01) however this may not provide any clinically relevant benefit. There were no significant differences in other outcomes.

Conclusions. In long-term tracheostomised patients weaning from ventilation, HFT resulted in significant improvements in oxygenation and modest increases in airway pressure when compared with LFT.

Paper to Practice. HFT may be a useful tool in weaning long-term ventilated ICU patients but requires further investigation before its role can be clearly established.
Delirium and dementia impact protein and energy intake in elderly hip fracture inpatients.

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Introduction. Malnutrition is a major predictor of poor outcomes following acute hip fracture. Patients with delirium or dementia may be at increased risk of poor intake post fracture leading to further nutritional decline. This study therefore aimed to explore the impact of delirium or dementia on protein and energy intake in elderly hip fracture inpatients.

Methods. As part of a larger study investigating barriers and facilitators to nutrition care in acute hip fracture, 24-hour adjusted weighed food records were available to compare protein and energy intake in delirious or demented versus non-delirious, non-demented inpatients. Diagnoses were made by the treating geriatrician. Weighed food records were completed and analysed by a single senior dietitian.

Results. A convenience sample of 116 randomly selected weighed food records was available across 82 acute hip fracture inpatients. Patients were predominantly community dwelling (72%), elderly (82.2 years), female (70%), malnourished (51.0%) and prone to co-morbidities (median 5). Surgical intervention was timely for the majority of patients (median D1). Patients with delirium or dementia had significantly reduced total protein (45 v 57 g; p = 0.049) and total energy (3911 v 5246 kJ; p = 0.012) intake compared with those without a diagnosis or delirium or dementia.

Conclusions. Having a comorbid diagnosis of delirium or dementia substantially impacts protein and energy intake in acute hip fracture inpatients.

Paper to Practice. Hip fracture inpatients with delirium or dementia should routinely receive nutrition assessment to prioritize appropriate nutrition interventions. Further studies are warranted in other inpatient populations with delirium or dementia.
Effects of an ECMO Program on Statewide Referral Patterns and Outcomes in Patients with Acute Respiratory Distress Syndrome or Pneumonia

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Introduction. The effects of introduction of an adult ECMO service on case-mix, referral patterns and outcomes at hospital and regional level have not been well studied. Two hospitals commenced adult ECMO services for respiratory failure in Queensland in 2009 in preparation for the swine flu pandemic.

Methods. A retrospective observational study was undertaken using de-identified data from a binational adult intensive care registry. All patients aged 14 years and older admitted to an adult ICU in Queensland, Australia from January 1 2006 to December 31 2013 with a diagnosis of pneumonia or acute respiratory distress syndrome (ARDS) were included. The outcome variable was in-hospital mortality. A multilevel logistic regression model was used to account for trends over time, severity of illness using APACHE III J risk of death and hospital level variance.

Results. The sample consisted of 6917 admissions from 35 hospitals. The in-hospital mortality in those 14-65 years with no major comorbidity who were ventilated at the time of the worst blood gas and had an APACHE III score > 100 was 40% before the ECMO service and 19% after (difference 21% (95% confidence interval 2-40%) p= 0.03). The odds ratio for dying was 0.57 (0.36-0.89) in those aged less than 65 years without major comorbidity after the introduction of ECMO compared to before ECMO when controlling for severity of illness and trends over time. Significant changes in referral patterns occurred.

Conclusion. In hospital mortality decreased in adult ICU patients with ARDS or pneumonia aged less than 65 years without major comorbidity after the introduction of an adult ECMO service combined with advanced mechanical ventilation guidelines.

Paper to Practice. This study is one of the first to demonstrate a statewide mortality improvement in subsets of patients with ARDS and pneumonia.
"Brain Training”: Evaluating cognitive recovery in the acute phase of stroke

Ms Hannah Tehan¹, Associate Professor Anne Tolan², Dr Kate Witteveen², Professor Gerry Tehan¹, Dr Donna Pinsker³

¹University of Southern Queensland, Moorooka, Australia, ²Australian Catholic University, Brisbane, Australia, ³The Prince Charles Hospital, Brisbane, Australia

Introduction. Cognitive deficits resulting from a stroke can have long-term subtle impacts upon quality of life. Surprisingly, little research has been conducted that explores cognitive recovery during the first few weeks following a stroke and there no early-intervention programs currently exist to facilitate recovery during this acute phase, despite this being consistently demonstrated as a crucial period of recovery. The intent of the current research is to explore changes in behaviour that do or do not occur as a result of the repeated administration of a battery of neuropsychological and cognitive tests over a short period of time while stroke patients are in hospital in the early stages of recovery from their first stroke.

Methods. A battery of 4 neuropsychological tests and 4 bespoke cognitive tests was administered to a normative group of older participants (55-87years) and five stroke patients six times across a two-week period.

Results. Five case studies are reported that showed that not all patients showed recovery as measured by practice effects on the neuropsychological tests. In contrast, all showed marked improvement on the cognitive tests, such that all were within normal limits on the final testing session.

Conclusions. Repeated testing using neuropsychological tests provide a good measure of natural recovery. However, repeated exposure to cognitive tasks where dual task difficulty is systematically manipulated leads to substantial improvements in performance. The research shows that early interventions can be cognitively beneficial to stroke patients.

Paper to Practice. Interventions based upon cognitive tests were task difficulty is manipulated can substantially facilitate cognitive recovery in the acute phase of stroke.
Low levels of physical activity predict worse survival to lung transplantation and poor early post-operative outcomes

Dr James Walsh¹²³, Associate Professor Daniel Chambers¹², Dr Stephanie Yerkovich¹², Associate Professor Peter Hopkins¹², Professor Norman Morris¹³

¹The Prince Charles Hospital, Chermside, Australia, ²The University of Queensland, Brisbane, Australia, ³Griffith University, Gold Coast, Australia

Background: Physical activity level (PAL) is an emerging measure of functional performance in people with chronic respiratory disease. Currently there is little evidence evaluating the role of PAL in people being considered for lung transplantation. Study aims: (1) To describe the profile of PAL in lung transplant candidates, (2) To determine whether candidates’ demographic, respiratory function or exercise capacity measures predict PAL, (3) To determine the influence of pre-transplant PAL on survival to transplantation and early post-operative outcomes.

Methods: A prospective observational design was used. Participants undergoing lung transplant assessment in a single institution were recruited. PAL was measured using the SenseWear multi-sensor device and defined as total energy expenditure in twenty-four hours/basal metabolic rate. Candidates’ demographic, respiratory function, six minute walk distance, and quadriceps strength were assessed to determine their relationship to PAL.

Results: 146 participants (77 males, mean age 49 ± 13 years, PAL of 1.51 ± 0.31) were studied. Seventy-one participants were classified extremely sedentary (PAL <1.40), forty-nine participants’ sedentary (1.40 -1.69) and twenty-six participants’ active (≥1.70). Only higher DLco (β=0.005, p<0.001) was identified as an independent predictor of increased PAL. Using Cox survival analyses, the extremely sedentary cohort had poorer survival to transplantation (Hazard ratio (95% CI): 9.12 (1.10-75.34), p=0.040) and were the only identified risk factor of prolonged mechanical ventilation post-transplantation (1.98 (1.16-3.38), p=0.012).

Conclusions: Pre-transplant physical activity level is independent of most currently used measures of disease severity. This new information provides important prognostic information regarding survival to transplantation and early post-transplant outcomes.
Benchmarking sessile serrated adenoma prevalence

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Introduction. Sessile serrated adenomas (SSA) are a recently described subtype of colorectal polyp. They contribute disproportionately to the burden of colorectal carcinoma that develop in people after a recent colonoscopy, probably because they are obscure and left in situ. Gastroenterologists are slowly becoming familiar with the endoscopic features of these polyps, but reported prevalence rates remain low.

Methods. To benchmark a realistic prevalence, we assessed a 12-month cohort of 707 consecutive patients undergoing colonoscopy in a unit providing freely available examinations to people with NHMRC-promoted indications. An experienced gastroenterologist using state of the art white-light Olympus 190 colonoscopes performed all examinations. A pathologist with expertise in SSA reviewed all specimens.

Results. The prevalence of SSA was 20.1% and SSA represented 18.9% of all polyps removed. The average age of patients with SSA was 58 years, the same as for the total cohort. Of the 270 SSA, 177 (65.6%) were in the proximal colon and the mean size was 7.6mm. The average size of proximal SSA was 8.3mm versus 6.4mm in the distal colorectum (P<0.01). Patients with SSA were likely to have other polyps (mean of 4.1 polyps per patient). Of these, 42.9% were SSA and 57.1% were conventional.

Conclusions. SSA are much more prevalent than previous reports suggest. This study provides a contemporary and clinically relevant benchmark for high quality colonoscopy.

Paper to practice. Bowel cancers develop with alarming frequency in people enrolled in colonoscopy surveillance. Operator expertise contributes to this and likely reflects subtle polyps being overlooked. This benchmark result will allow colonoscopists to critically evaluate personal scores and hopefully lead to more reliable colonoscopy.
Improving Our Understanding of Pressure Injuries in Critical Care Patients

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1The Prince Charles Hospital, Chermside, Australia, 2Nambour General Hospital, Nambour, Australia

Introduction. Hospital-acquired pressure injuries (PI) are an important problem in acute healthcare facilities and the focus of national patient safety initiatives. Critical care patients are particularly vulnerable to PI. Hospitals are now fined for stage III and IV PI as a basis for performance improvement.

Methods. A descriptive study was performed using data from incident reporting systems, the Adult Intensive Care Unit (ICU) clinical database and the Queensland Hospital Admitted Patient Data Collection to identify the clinical characteristics of patients with PI, focusing on ICU patients with stage III, IV or suspected deep tissue injury.

Results. From July 2006 to March 2015, after potential duplicates were eliminated, there were 5280 PI incident reports in 3860 patients. Incident reports of both present on admission and hospital acquired PI increased over time. There were 44 incident reports of severe PI not present on admission in 22 ICU patients. There were 13 ICU patients (11 stage III, 2 stage IV PI) recorded as potentially subject to fines. Of these 13, all required pharmacological support with at least 2 inotrope/vasopressor agents, all had sequential organ failure assessment (SOFA) scores greater than 5, 7 had acute renal failure requiring renal replacement therapy and 5 were on extracorporeal life support. The average ICU length of stay for this group was 40 days. Five of 13 died, seven were transferred to other hospitals and one was discharged home from hospital. All 13 patients had been reported on the incident monitoring database although the reported stage was not severe in 7.

Conclusions: Extreme severity of illness rather than deficiencies in quality of care should be considered in critical care patients with hospital acquired severe PI.

Paper to Practice. This study links data from multiple sources to better understand the aetiology of severe PI in ICU patients.
Examining microvascular perfusion pre and post cardiac surgery

Ms Amy Spooner, Mr Kimble Dunster, Dr Daniel Mullany, Ms Amanda Corley, Mrs Tatum Cobb, Miss Megan O’Keeffe, Mrs Tracy Nowicki, Dr Chris Anstey, Mrs Peta McKay, Prof Paul Fulbrook, Mr Paul McCormack, Mr Oystein Tronstad, Mr Lawrence Caruana, Mrs Elissa Robins, Dr John Moore, Professor John Fraser

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Introduction. Pressure injuries (PIs) remain a major health problem globally. In Queensland, PIs are considered preventable, incurring fines (up to $50 000) if hospital-acquired. Despite modern PI prevention strategies to minimise shear, friction and pressure, PI incidence remains high. Skin perfusion is under-recognised as we lack an objective “test” to determine early signs of perfusion failure resulting in PIs. This prospective observational study uses a novel approach to examine skin perfusion in cardiac surgical (CS) patients admitted to intensive care (ICU).

Methods. Skin perfusion (heels and sacrum) in healthy subjects, low-risk and high-risk CS patients was examined using laser Dopplers and thermal imaging cameras pre and post-operatively. Demographic data, PI risk tools (Waterlow and Braden), patient management (medications, positioning) and premorbid factors (nutrition and mobility status) were also collected. Demographic and PI risk scores are expressed as means.

Results. 82 patients have been recruited currently. Preliminary results indicate that age and BMI were similar between low-risk and high-risk CS patients. As expected high-risk patients had longer cardiopulmonary bypass (CPB) times (147mins:92mins, p-value<0.05). Four patients developed PIs (three low-risk, one high-risk patient) and these patients had extended ICU (2 days:23 days, p-value<0.0001) and hospital lengths of stay (13 days:58 days, p-value<0.0001) when compared to non-PI patients. CPB times were longer in PI patients, although not statistically significant. The Waterlow appeared to be a better predictor of PIs preoperatively than the Braden tool.

Conclusions. This study showed high-risk CS patients had longer CPB times. Although patients that developed PIs were predominantly low-risk, these patients had extended ICU and hospital lengths of stay.

Paper to Practice. These findings will give insight into the complex pathophysiology of PIs, inform the development of preventative strategies to minimise skin failure and reduce the financial and debilitating consequences of PIs upon patients.
Fluid resuscitation and blood transfusion result in higher vasopressor requirements in an ovine model of endotoxemic shock

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Introduction. Volume resuscitation remains the first line therapy for septic shock despite limited evidence supporting its use. There is increasing concern regarding both its efficacy and safety with observational adult data suggesting improved outcomes with lower volumes of fluids and paediatric literature suggesting a delayed paradoxical worsening of shock after fluid resuscitation.

By comparing the noradrenaline requirements in the 12 hours after volume resuscitation this study aims to establish if volume resuscitation effectively improves shock and sepsis induced hypotension.

Methods. Fifteen sheep underwent anaesthesia, intubation and mechanical ventilation prior to induction of endotoxemic shock. Shock was induced utilising a 4hr infusion of endotoxin. Animals then received one of 3 resuscitation modalities, saline resuscitation 40mls/kg (SR), 2 units of PRBCs (BR) or no volume resuscitation (NR). Animals were then monitored for 12 hours, receiving protocolised haemodynamic support with noradrenaline/vasopressin to maintain a target MAP of 60-65mmHg. Noradrenaline was instituted when the MAP decreased below 60mmHg. Vasopressin was introduced when the noradrenaline dose reached 20mcg/min at a maximum dose of 1.8units/hr.

Results. Mean weights did not differ significantly between (39.88kg for NR, 46.4kg for SR and 39.6kg for BR).

Mean noradrenaline dose of SR (83.7mcg/min) and BR (66.85mcg/min) was compared to NR (34.21mcg/min) using one-way ANOVA with adjustment for multiple comparisons. Both SR and BR resulted in statistically significantly increased noradrenaline requirements, with mean differences of 49.5mcg/min (CI 27.18–71.81) and 32.64mcg/min (CI 17.22 – 48.06) respectively.

Conclusions. Volume resuscitation with 0.9% saline or PRBCs is ineffective in reversing sepsis induced hypotension and results in an increased requirement for vasopressor support in the following 12 hours in this model of endotoxemic shock.

Paper to Practice. This study suggests volume resuscitation in sepsis is ineffective in treating hypotension and results in delayed iatrogenic worsening of shock. This supports the similar findings in the paediatric literature.
β2- and β1-adrenoceptor mediated spontaneous contractions in human heart in patients with terminal heart failure

**Introduction.** Approximately 30-50% of heart failure patients die of sudden cardiac death caused by a ventricular arrhythmia. Characteristic features of heart failure, namely increased sympathetic nerve-β-adrenoceptor (AR) activity and structural remodeling of the heart, combine to initiate ventricular arrhythmias that can be fatal. There are two cardiostimulatory βARs, β1AR and β2AR. There are contrasting views concerning β2ARs in heart failure with respect to whether they have a protective or harmful role. Both β2AR and β1AR couple to the stimulatory Gsα-protein-cyclicAMP-protein kinase A (PKA) pathway in human heart. We therefore hypothesized that activation of both β2AR and β1ARs in human heart could cause spontaneous contractions. Since cyclicAMP is metabolized and inactivated by phosphodiesterases (PDEs) we sought to determine their role in ventricular arrhythmias.

**Methods.** Right ventricular trabeculae from freshly explanted hearts of 18 patients with terminal heart failure were obtained. Spontaneous contractions induced by (-)-noradrenaline, mediated through β1ARs (β2ARs blocked with ICI118551), and (-)-adrenaline, mediated through β2ARs (β1ARs blocked with CGP20712A) were assessed in the absence and presence of PDE3 (cilostamide 100 nM) or PDE4 (rolipram 10 μM) inhibitors.

**Results.** (-)-Noradrenaline caused spontaneous contractions at concentrations greater than 20 μM (P < 0.05). Inhibition of PDE3 or PDE4 lowered the threshold concentration of (-)-noradrenaline to 600 nM (P < 0.05). (-)-Adrenaline caused spontaneous contractions at concentrations of greater than 200 μM (P < 0.05). Inhibition of PDE3 or PDE4 lowered the threshold concentration of (-)-adrenaline to 6 μM (P < 0.05).

**Conclusions.** Activation of both β1AR and β2AR cause spontaneous contractions in an experimental model of human ventricular arrhythmia. Both PDE3 and PDE4 reduce their occurrence.

**Paper to Practice.** These studies show the importance of blocking β2AR in addition to β1AR to reduce the likelihood of catecholamine induced ventricular arrhythmias in patients with heart failure.
ECMO therapy with blood transfusion attenuates myocardial inflammation and injury in an ovine model of S-ALI

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Introduction: Extracorporeal membrane oxygenation (ECMO) has been used to treat respiratory failure secondary to smoke inhalation in humans. Blood transfusion is an essential part of ECMO therapy; however, packed red blood cells (PRBC) acts to activate the polymorphonuclear neutrophils to cause inflammation and organ dysfunction. This study investigated whether the transfusion of ovine PRBC causes ECMO inflammation leading to heart tissue injury in an ovine model of smoke-induced acute lung injury (S-ALI) during ECMO therapy.

Methods: Sixty sheep were randomised into eight groups. S-ALI groups were those receiving mechanical ventilation (MV), ECMO with no transfusion for 2 or 24 hr (SE2H; SE24H) or ECMO with fresh/aged blood transfusion (SEF24H/SEA24H) and monitored for 24 hours. Sham controls were healthy sheep receiving MV (HC) or on ECMO for 2 or 24 hr (E2H; E24H). Both left and right hearts ventricular were removed for histological examination upon completion of the study to evaluate heart tissue structure, cell morphology, and inflammatory cells infiltration.

Results: Sheep treated with ECMO (E2H and E24H) and S-ALI (SC) significantly experienced greater inflammatory cells infiltration in the interstitium (P<0.05) and blood vessels (P<0.01) of both left and right ventricles when compared to healthy controls (HC). No difference in the presence of inflammatory cells infiltration in interstitium and blood vessels were noted in ECMO transfusion groups with S-ALI (SEF24H and SEA24H). However, heart tissue edema and enlargement of cardiomyocytes (P<0.05) were observed in SEA24H and SEF24H, respectively.

Conclusions: These data indicated that ECMO therapy and S-ALI contribute directly to myocardial inflammation and tissue injury and that PRBC regardless of age exacerbates the cellular injury caused by ECMO.

Paper to Practice: These data may help to improve the survival rate of patients treated with ECMO and enlighten clinicians the potential risks of blood transfusion for critically ill patients on ECMO.
Using lung microdialysis to describe the pharmacokinetics of inhaled antibiotics in mechanically ventilated sheep

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¹Critical Care Research Group, Chermside, Australia, ²Burns Trauma and Critical Care Research Centre, Herston, Australia

Introduction
Pneumonia is a very common condition in the critically ill patient population. The poor lung penetration of many systemically administered antibiotics is thought to predispose to the emergence of multiresistant organisms. Inhaled antibiotics could achieve higher lung antibiotic concentrations without causing systemic toxicity. The aim of this study was to compare the plasma and lung concentrations of inhaled and intravenously administered tobramycin and lincomycin in healthy ventilated sheep.

Methods
We used the microdialysis technique to study the pharmacokinetics of inhaled antibiotics in the interstitial fluid of the lungs of healthy ventilated sheep (n=10). Half (n=5) received intravenous and the other half received inhaled antibiotics. The antibiotics used were tobramycin and lincomycin. Microdialysis catheters were placed in the lungs and in the internal jugular vein. Sampling was done 20 minutely and assayed for the antibiotics.

Results
Interim data shows significant differences (60-80 fold) in the antibiotic concentrations in the lungs when delivered by inhaled route compared to that when delivered by the intravenous route. (Figure 1)

Conclusion
Microdialysis is a valid technique to study the PK of inhaled antibiotics. Inhaled drugs could now be studied using this technique. PK data thus obtained would be useful to guide correct dosing schedules. This could improve patient outcomes and cost of health care.

Figure 1: Comparison of antibiotic concentration in the lung tissue when delivered by intravenous route and inhaled route. (LCM- Lincomycin, TMC- Tobramycin)
Buffy coat pooled ovine platelet units: validation and characterisation for transfusion research

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Introduction: Platelet concentrates (PCs) are transfused to control the risks of bleeding; yet their possible contribution to the risks associated with transfusion remains poorly understood. Our group therefore aims to develop ovine (ov) models of PC transfusion to complement our existing models of red cell transfusion. This study aimed to validate the production of buffy coat (BC) pooled ovPCs, characterise storage-related changes and compare these to human (hu) PCs.

Methods: OvPCs (n=5) were prepared from 4 compatible BC pooled units with minor modifications to standard procedures. Briefly, platelet-rich BCs were pooled, mixed with SSP+ additive solution, separated by centrifugation, leucodepleted by filtration and stored in the associated platelet storage bag. OvPCs and equivalent huPCs (n=5) provided by the Australian Red Cross Blood Service were stored for 5 days at 22°C with agitation and underwent testing on days 2, 3 and 5. Biochemical parameters were evaluated using blood-gas analyser, platelet activation markers were tested by flow cytometry, and platelet function was assessed by Multiplate using ADP and collagen activators.

Results: All ovPCs met quality control specifications for huPCs. While some differences were observed in initial characteristics of ovPCs and huPCs, during storage the changes in biochemistry, platelet function and platelet activation were similar. Notably the magnitude of decreased ADP and collagen aggregation were more severe for ovPCs and the increased CD62P expression less severe.

Conclusions: Production of BC pooled ovPCs is feasible and results indicate that storage-related changes in ovPCs are comparable to huPCs.

Paper to practise: Based upon similarities described here, sheep will provide a suitable model in which to investigate the risks associated with PC transfusion.

Table 1. Testing of ovPCs and huPCs (mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ovPCs (n=5)</th>
<th>huPCs (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D2</td>
<td>D5</td>
</tr>
<tr>
<td>Biochemical changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.16±0.01</td>
<td>7.17±0.05</td>
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<tr>
<td>Glucose [mmol/L]</td>
<td>5.18±0.37</td>
<td>3.32±0.69</td>
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<tr>
<td>Lactate [mmol/L]</td>
<td>6.26±3.19</td>
<td>5.54±2.34</td>
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<tr>
<td>pCO₂ [mmHg]</td>
<td>17.02±1.89</td>
<td>7.08±1.19</td>
</tr>
<tr>
<td>pO₂ [mmHg]</td>
<td>187±2.55</td>
<td>187±6.50</td>
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<tr>
<td>Platelet function</td>
<td></td>
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<tr>
<td>ADP – Aggregation [AU]</td>
<td>64.48±42.77</td>
<td>25.22±30.33</td>
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<tr>
<td>Collagen – Aggregation [AU]</td>
<td>37.78±36.03</td>
<td>18.76±21.08</td>
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<tr>
<td>Platelet activation</td>
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<tr>
<td>Annexin V [%]</td>
<td>15.44±7.48</td>
<td>24.10±9.34</td>
</tr>
<tr>
<td>CD62P [%]</td>
<td>25.96±3.54</td>
<td>30.24±2.82</td>
</tr>
</tbody>
</table>
Microbial concordance post-lung transplant is associated with a skew towards an M1 macrophage phenotype

Dr Stephanie Yerkovich¹, Mr Ricky Nelles¹, Mrs Maxine Tan¹, Mr Luke Samson¹, A/Prof Peter Hopkins¹, A/prof Daniel Chambers¹
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Introduction. Chronic lung allograft dysfunction (CLAD) remains one of the main barriers to long-term survival following lung transplantation. We have previously identified that re-colonization of the allograft (concordance) with Pseudomonas was not associated with CLAD, while de novo acquisition (discordance) was associated with CLAD. The mechanisms associated with this are unknown. Macrophages can be broadly classified as M1 (pro-inflammatory) or M2 (wound healing and pro-fibrotic). We hypothesized that microbial concordance between the pre- and post-lung transplant microbiome would be associated with reduced innate immunity and a predominance of M1 polarised macrophages in the lung.

Methods. This was a cross-sectional study performed on stored bronchoalveolar lavage (BAL) samples. Pre- and post-transplant bacterial cultures were used to classify patients into concordant or discordant microbiome groups. BAL cellularity was determined, markers of innate immune activation (mannose-binding lectin (MBL), IL-1β, IL-6, IL-8, IL-10, TNFα, TGF-β) and M1 (TNFα, IL-1β, IL-6, NOS, ICAM-1) and M2 (IL-10, arginase, TGF-β, CD36, macrophage scavenger receptor 1 (MSR1)) macrophage subtypes were assayed.

Results. There was no association between any patient demographic (time post-transplant, age, pre-transplant diagnosis) and any outcome measure. There was no association between any innate immune cytokine or BAL cellularity and microbial concordance (p>0.05). A concordant microbiome was associated with increased levels of ICAM-1 (p=0.011), TNFα (p=0.001), and NOS2 (p=0.031), all markers associated with an M1 macrophage phenotype, and IL-10 (p=0.008), an M2 macrophage associated marker.

Conclusions. Microbial concordance is associated with a skew towards an M1 macrophage pattern. There was no evidence of altered innate immune system activation.

Paper to Practice. This identification of a M1 macrophage skew will allow future diagnostic tests to assess for M1 macrophage predominance during the assessment of lung allografts and further studies will investigate M1 macrophage functionality.
Reliability of thermodilution derived cardiac output with different operator characteristics

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Introduction. Cardiac output (CO) is measured clinically using the thermodilution method (TM) at right heart catheterisation (RHC). This method is operator dependent; however studies validating the TM do not discuss operator variability. We aimed to evaluate intra-operator variability on CO measurement using the TM in a previously validated mock circulation loop (MCL).

Methods. Physicians experienced with RHC measured four different CO settings of a MCL using the TM. CO of the mock circulation loop was randomly adjusted through variations in heart rate, contractility and vascular resistance with participants blinded. Participants were instructed to perform a minimum of three measurements such that each CO measurement was within 10% of each other and confirm they were satisfied with the measurement. Specialty (intensive care or cardiology), age, gender, body mass index (BMI), grip strength and number of previous RHCs were recorded. A standard linear regression model was used in the analysis.

Results. There were 15 participants (10 male and 5 female). Results are presented as mean (SD): Age 37.7 (4.4) yrs, BMI 26.4 (5.4) kg/m², grip strength 42.3 (10.1) kg. Participants tended to overestimate CO with a mean difference of +0.75 (0.71) L/min. Overall R² = 0.85 for actual vs measured CO. Operator experience was the only variable predictive of CO measurement accuracy (p = 0.001). The kappa values for inexperienced (10 – 25 prior RHC) and very experienced (> 100 prior RHC) operators were 0.01 and 0.37 respectively.

Conclusions. CO measurement using the TM was generally close to actual CO, with a trend toward overestimation. RHC operator experience is the only variable predictive of CO measurement accuracy.

Paper to Practice. This study provides clinicians with a guide on the expected error range associated with using the TM for CO measurement and encourages clinicians to practice this technique extensively to improve measurement accuracy.
In-vitro Comparison of Physiological Control Systems for Rotary LVADs

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**Introduction.** Rotary blood pumps (RBPs) are used to support the heart while waiting for a transplant. However, RBPs are clinically operated at a constant speed (CS) and have an unphysiological response to changes in preload and afterload when compared to the native heart, which may result in ventricular suction or pulmonary congestion. Many RBP physiological control systems, which automatically adjust RBP speed based on patient demand, have been reported in literature but a comparative study has never been done. Therefore, this study aimed to compare several physiological control systems to determine which control strategy is ideal for patient support.

**Methods.** Physiological control systems evaluated in this study included those that are based on Starling-like control using left ventricular end-diastolic pressure (SL-LVEDP), constant inlet pressure (CIP), constant afterload (CA), constant flow (CQ), and a compliant inflow cannula (CIC) which passively alters RBP inlet resistance as inlet pressure changes. Each system was evaluated and compared to CS under simulated exercise conditions and vascular resistance changes using a mock circulation loop simulating RBP-supported left heart failure.

**Results.** During increased pulmonary vascular resistance (500 dyne.s.cm\textsuperscript{-5}) and decreased systemic vascular resistance (600 dyne.s.cm\textsuperscript{-5}), the SL-LVEDP, CIP and CA systems all automatically adjusted RBP speed, and thus flow, to prevent ventricular suction and pulmonary congestion. However, ventricular suction occurred with CQ and CS modes. During exercise, SL-LVEDP, CIP and CA controllers increased RBP flow the most (4-5 L/min), thus increasing exercise capacity.

**Conclusions.** SL-LVEDP, CIP and CA systems responded the best by eliminating ventricular suction and pulmonary congestion while increasing exercise capacity through increases in flow.

**Paper to Practice.** Physiological control systems based on SL-LVEDP, CIP or CA techniques may benefit heart failure patients by reducing complications and providing increased quality of life.
Tissue integration of a suture-less inflow cannula using melt electrospun bilayer scaffolds

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Introduction. Rotary blood pump implantation typically requires extensive suturing while on cardiopulmonary bypass, which is associated with complications such as postoperative bleeding and end-organ dysfunction. A suture-less inflow cannula has been developed which seals via myocardial compression and does not require bypass. There is a risk of tissue necrosis due to the compression, thus permanent tissue integration of the suture-less inflow cannula with the heart tissue is required. This study aimed to promote tissue integration on a suture-less inflow cannula using a bilayered scaffold.

Methods. The bilayered scaffold was made by melt electrospinning PCL onto curing silicone. Analysis of biocompatibility of the bilayered scaffolds was undertaken with in-vitro assays to study cell attachment (live/dead staining), proliferation (MTT assay) and morphology using fluorescent cell labelling (DAPI/Phalloidin) and scanning electron microscopy.

Results. Cell analysis indicated the bilayered scaffold was able to support cell attachment and proliferation, and the cells exhibited healthy morphology and no cytotoxicity was found by using PCL and silicone together.

Conclusions. The bilayered scaffold indicated good potential for use with the suture-less inflow cannula to allow neointima formation around the cannula after implantation, ultimately resulting in an integrated suture-less inflow cannula.

Paper to Practice. Clinical significance of this study is that after implantation of the suture-less inflow cannula, fibrous tissue is able to infiltrate the bilayered scaffold which can act as a safety barrier in case of tissue necrosis and may reduce the incidence of thrombus formation.
Hyperoxaemia partially preserves collagen-dependent platelet function during extracorporeal membrane oxygenation

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Introduction: TPCH is Queensland’s preeminent centre for extracorporeal membrane oxygenation (ECMO), a life sustaining system for patients with refractory cardio/respiratory failure. An array of complications are recognised during ECMO. Haemorrhagic and thrombotic events are notable with patients exposed to number of physiological insults which affect platelets, fibrinogen and coagulation factors. Among these insults, the impact of hyperoxaemia is poorly understood.

Methods: Four Marquet PLS ECMO circuits were set up in closed ex-vivo loops and circulated with 450mL of fresh, whole human blood from volunteer donors. After four hours, circuits were separated into test groups; either normoxaemia (PaO2 <150mHg) (n=2) or hyperoxaemia (PaO2 >500mmHg) (n=2). Five time points for blood sampling were used: t=0 (before blood was introduced into the circuit), t=5min t=4h t=10h and t=28h. Testing included FBC, ABG, platelet aggregometry (Multiplate) and thromboelastometry (ROTEM).

Results: Platelet count initially declined by 30-40% in all circuits due to haemodilution but remained unchanged thereafter. Collagen-dependent platelet function progressively declined throughout the experiment in both normoxaemia and hyperoxaemia groups (figure 1). However at 28 hours, no collagen-dependent activity remained in any of the normoxaemia circuits. Conversely, approximately 10% of baseline activity remained in hyperoxaemia circuits.

Conclusions: Platelet activity progressively declines following initiation of ECMO, a trend partially abated by hyperoxaemia. Further investigation is required to ascertain the risks and benefits of hyperoxaemia.

Paper to Practice: The findings demonstrate that patients receiving ECMO need careful consideration and monitoring of platelet function with the knowledge that changes to PaO2 may affect thrombotic and haemorrhagic risk.